Voxel-Wise Balloon Model Parameter Estimation from BOLD Time Series

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Introduction

fMRI signal changes using blood oxygenation level dependent (BOLD) contrast reflect the complex interplay of neuronal and hemodynamic events. Using a physiologically based model for BOLD contrast dynamics known as the "Balloon Model [1-6]," we attempt to address how hemodynamic effects can be extracted from the BOLD response in humans. BOLD contrast dynamics have been shown to behave in a nonlinear manner in the stimulus duration (SD) range of less than 2 sec. This observed nonlinearity (NL)[8,9,10], which also varies considerably over space[9], may be due to neuronal or hemodynamic effects or a combinaton of both. Using the Balloon model, we address if purely hemodynamic effects can account for this NL. To do this, we varied stimulus durations within a run and forced the balloon model to fit all stimulus durations within a voxel using the same balloon parameters.

The Balloon Model

For a given flow of blood into the venous compartment, the three Balloon parameters which control the hemodynamic contribution to the BOLD signal are thought to be E_0, V_0, and Gam[2]. E_0 represents the fraction of total hemoglobin not bound to O_2; $v(t)$ is the fraction of voxel volume filled with blood during the active state normalized to that at rest, V_0; Gam is the exponent defining the relationship between venous outflow and fractional blood volume; τ_o is the mean venous transit time of blood in the venous compartment; $q(t)$ is the total voxel content of dHB during the active state normalized to that at rest; viscos is a viscosity term that varies between viscup, during balloon inflation, and viscdown, during balloon deflation. On a voxelwise basis, the stimulus waveform was smoothed (WAVrisetime), scaled (FLINamp), and phase shifted (FLINdelay) in order to generate an optimal curve, ShiftedFlowIn(t), representing blood flow into the venous compartment.

Gam >= 2 | Larger NL | Smaller NL
τ | Longer | Shorter
E_0 | Smaller | Larger

Dilution Effects Increase FlowIn > Flowout
Washout Effects Increase FlowOut > FlowIn

Physiological Parameter Contribution to NL

$2 << Gam << 4$ ($\tau >> (E_0 > Gam)$)
$Gam \approx 4$ ($\tau \approx E_0) >> Gam$)
$4 << Gam < 8$ ($E_0 >> (\tau > Gam)$)

Relevant Physiologic Range [1,3]

E_0 0.2 to 0.4
V_0 0.02 to 0.05
Gam 2.1 to 6.4

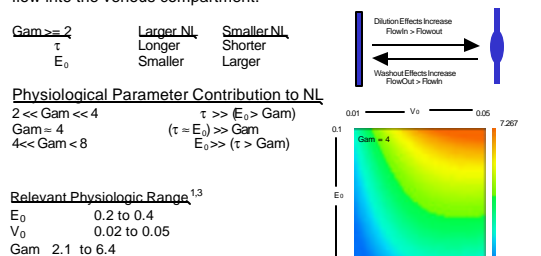Figure 1: NL Map at 1.5 T
E_0, dHB fraction; V_0, blood volume fraction at rest; Gam, steady state venous outflow-volume relationship

For TE = 30ms

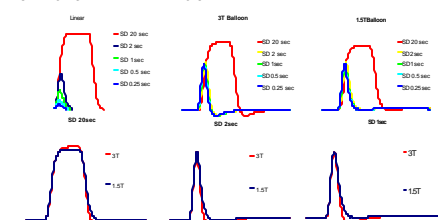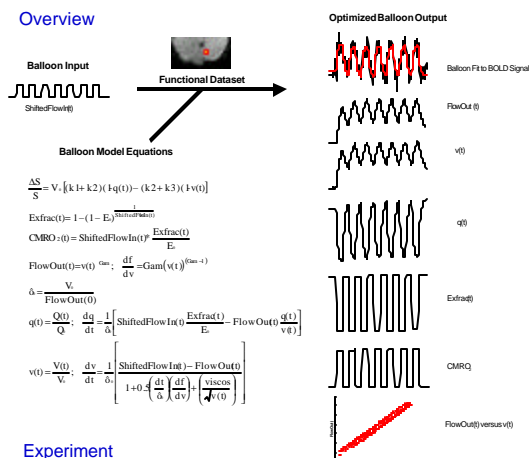|	1.5T	3.0T
k1	$5.2 * E_0$	$10.4 * E_0$
k2	$1.43 * E_0$	$0.5 * E_0$
k3	0.43	-0.5

Figure 2:
Balloon Curves at different Tesla, SD = 20 sec.
$V_0 = 0.03$, $E_0 = 0.3$, and Gam = 2.6

Purpose

To determine if human BOLD signal nonlinearities (NL) can be fully described by the Balloon model.

Methods

Overview

Balloon Input
ShiftedFlowIn(t)

Functional Dataset

Balloon Model Equations

Optimized Balloon Output
- Balloon Fit to BOLD Signal
- FlowOut (t)
- v(t)
- q(t)
- Exfrac(t)
- CMRO₂
- FlowOut(t) versus v(t)

$$\frac{\Delta S}{S} = V_o \left[(k1 + k2)(1 - q(t)) - (k2 + k3)(1 - v(t)) \right]$$

$$Exfrac(t) = 1 - (1 - E_0)^{\frac{1}{ShiftedFlowIn(t)}}$$

$$CMRO_2(t) = ShiftedFlowIn(t) * \frac{Exfrac(t)}{E_0}$$

$$FlowOut(t) = v(t)^{\frac{1}{Gam}}; \quad \frac{df}{dv} = Gam(v(t))^{(Gam-1)}$$

$$\hat{o} = \frac{V_o}{FlowOut(0)}$$

$$q(t) = \frac{Q(t)}{Q}; \quad \frac{dq}{dt} = \frac{1}{\hat{o}}\left[ShiftedFlowIn(t)\frac{Exfrac(t)}{E_o} - FlowOut(t)\frac{q(t)}{v(t)} \right]$$

$$v(t) = \frac{V(t)}{V_o}; \quad \frac{dv}{dt} = \frac{1}{\hat{o}_+}\left[\frac{ShiftedFlowInt(t) - FlowOut(t)}{1 + 0.5\left[\left(\frac{dt}{\hat{o}}\right)\left(\frac{df}{dv}\right) + \frac{viscos}{\sqrt{v(t)}}\right]} \right]$$

Experiment

The stationarity of the model parameters across stimulus timing was assessed using a visual task consisting of an 8 Hz flashing checkerboard. The visual stimuli were presented at durations of 1000ms, 2000ms, 4000ms, and 16 sec. Standard deviations of each stimulus duration epoch were matched to prevent biasing our fitting routine. Images were also acquired in a blocked trial (BT) paradigm, alternating 30s periods of stimulation with 30s periods of rest.
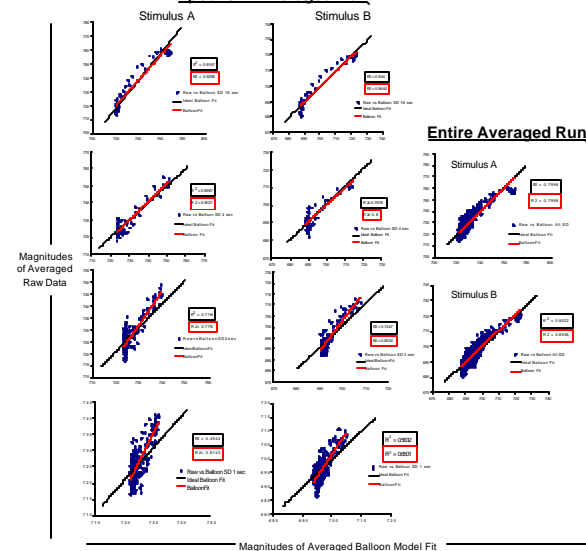
During these tasks, a series of axial 510 echo-planar images (EPI) of the visual cortex were acquired on a 3T GE Signa (Waukesha, WI, USA) magnet, with a 24cm field of view, 5mm slice thickness, and 64x64 matrix size. (TR: 1000ms, TE: 30ms). Each run was performed twice to assess the repeatability of the fitted parameters. To achieve the best least squares fit to BOLD signal on a voxelwise basis, balloon model parameters were varied independently by using a balloon signal model, Inflater, as a plugin for the nonlinear simplex fitting routine, 3dNLfim, packaged with AFNI[11]. A linear noise model, with a constant and linear term, was incorporated into the fitting procedure. The highest correlated BT voxels in visual cortex were included in the functional averaging analysis for stimuli A and B. Data from 2 subjects were acquired. Each showed similar results.

Stimulus | Voxelwise Analysis | Response
A | Inflater |
B | Functional Dataset |
Avg Balloon Fit — Avg Raw

Results

	A1	A2	Mean	StdDev	%StDev/Mean	B1	B2	Mean	StdDev	%StDev/Mean
constant	726.422	719.873	723.148	4.631	0.640	687.650	695.451	691.551	5.516	0.798
linear	-0.008	0.029	0.011	0.026	241.779	0.023	0.005	0.014	0.013	94.457
FLINamp	0.598	0.491	0.545	0.076	13.938	0.582	0.603	0.592	0.015	2.498
FLINdelay	-0.794	-0.808	-0.801	0.010	-1.227	0.662	0.545	0.604	0.083	13.748
Vo	0.051	0.049	0.050	0.002	3.825	0.034	0.041	0.037	0.004	12.007
Eo	0.330	0.295	0.312	0.025	7.982	0.436	0.393	0.415	0.030	7.288
Gam	4.151	3.723	3.937	0.303	7.687	3.742	3.495	3.618	0.175	4.830
WAVrisetime	2.572	2.788	2.680	0.153	5.706	2.431	2.625	2.528	0.138	5.445
viscup	3.780	3.206	3.493	0.406	11.620	8.529	7.115	7.822	1.000	12.782
viscdown	8.870	11.086	9.978	1.567	15.704	9.945	10.250	10.098	0.215	2.133

Table 1: Balloon Model Parameter Estimation

Epochs in Averaged Run

Stimulus A | Stimulus B

Entire Averaged Run

Stimulus A
Stimulus B

Magnitudes of Averaged Raw Data

Magnitudes of Averaged Balloon Model Fit

Figure 3: Raw Experimental Data versus the Optimal Balloon Model Fit
The magnitudes for different stumuli (A and B), averaged across two runs, are plotted for epochs (16, 4, 2, 1 sec) within an averaged run and for all epochs in the averaged run).

Conclusions

Balloon model hemodynamics do not fully account for human BOLD signal NL.

Within a run for a given stimulus, epochs of longer stimulus duration are better characterized by the Balloon model than shorter stimulus durations.

As epoch durations become briefer, the Balloon model fits increasingly become more linear relative to experimental data and, at the same time, more nonlinear relative to a linear model.

References

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